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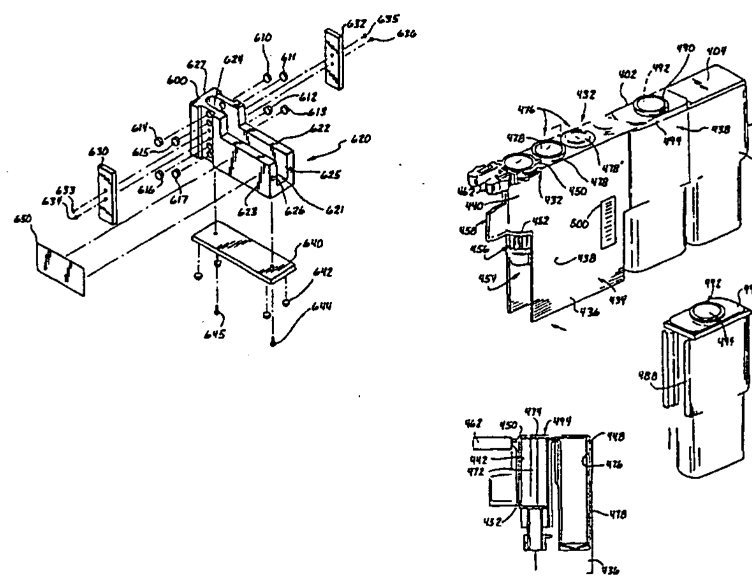

(57) Abstract

There is provided a device, apparatus and methods for suspending magnetic particles retained within a container. In a particular application, magnetic particles which have become settled and even agglutinated at the lowest point, with respect to gravity, in the container, are magnetically pulled from this position, preferably to a sidewall of the container, whereby upon cessation of application of the magnetic force to the container, the particles will no longer be settled and/or agglutinated. In those containers having a fluid contained therein, the magnetic particles can then be easily suspended in the fluid. In a particular embodiment, the container is a vial retained within a cartridge for use in an automated assay apparatus.

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MAGNETIC PARTICLE SUSPENDING DEVICE, APPARATUS AND METHODS FOR USING SAME

Field of the Invention

The present invention relates to a device, apparatus and methods for suspending, typically in a fluid, magnetic particles which have become settled at the bottom of a, typically fluid-containing, container.

Background of the Invention

The use of magnetic particles for performing steps, such as separating steps for various biochemical operations, including immunoassays, such as medical diagnostic assays is known in the art. In a particular application, biochemical assays are carried out in automated devices, which utilize cartridges, typically disposable cartridges. The cartridge may include one or more containers, such as a vial or vials, which contain various reagents used in carrying out a particular assay. At least one of the vials contains a fluid and magnetic particles or superparamagnetic particles, which, while not themselves magnetic, are attractable by a magnetic force.

During storage of the cartridge the magnetic particles under the influence of gravity, settle to the lowest point, with respect to gravity, of the vial. After a period of time, the magnetic particles can be quite compactly settled and actually agglutinated on the bottom of the vial. The agglutinated magnetic particles must be suspended in the fluid before the cartridge can be used for performing a particular assay. Typically, cartridge users, in order to suspend the agglutinated magnetic particles, have resorted to shaking, or otherwise physically agitating the cartridge and/or vial, for example, by vortexing them. However, these suspension techniques result in undesirable foaming and/or bubbling of the fluid contained in the vial and in subsequent fluids to which the fluid in the vial may be added. This

foaming and/or bubbling of the fluid in the vial interferes with subsequently required assay steps and necessitates further inconvenient, time-consuming steps to remove the bubbles and/or foam from the fluid. For example, such steps may include tediously pipetting the bubbles and/or foam from the surface of the fluid in the vial. Additionally, the foaming results in loss of reagent and the need to insert instruments, such as pipettes, into the vial can increase the risk of contamination of the contents of the vial.

Accordingly, it would be desirable to provide a magnetic particle suspending device, apparatus and related methods for suspending magnetic particles, particularly, those magnetic particles which have become compactly settled and even agglutinated on the bottom of a container, such as a vial, wherein the device, apparatus and related methods do not otherwise disturb the fluid in the vial, thereby avoiding foaming and/or bubbling and the attendant inconvenient and time-consuming steps required to remove such bubbles and/or foam, loss of reagent and increased risk of contamination.

Summary of the Invention

In accordance with one aspect of the present invention there is provided a magnetic particle-suspending device for suspending settled magnetic particles. The magnetic particles are contained in a fluid-containing vial. The vial has an interior portion and an exterior portion. The vial also has an interior bottom portion and an interior side wall portion. The vial is contained in a cartridge. The cartridge has a first side portion, a second side portion, a top portion, a base portion, a forward portion and a rear portion. The device includes at least one magnet disposed adjacent to the device. The magnet is disposed to provide a magnetic force on at least two separate points on the interior portion of the vial. The device also includes means for positioning the cartridge and the magnetic particle containing vial in relation to the at least one magnet. The positioning means provides for the repeatable, fixed positioning in three dimensions of a cartridge in relation to the magnet. Such positioned placement of the cartridge in

the device causes at least some of the magnetic particles settled in the interior bottom portion of the vial to be adhered on an interior portion of the vial, other than the interior bottom portion of the vial.

In a particular embodiment, the positioning means includes at least one surface opposable against and shaped for at least partial mating engagement with a side portion and a forward portion or a side portion and a rear portion or a side portion and a top portion of the cartridge.

In another embodiment of the present invention, the device further includes a second magnet disposed adjacent to the means for engaging the cartridge. The magnet can be a permanent magnet or an electromagnet. In a preferred embodiment the polarity of the two or more magnets directed towards the magnetic particles is the same.

In yet another embodiment, the device includes either a slot allowing access to a driven means on the vial or a driving means to engage the driven means on the vial.

In a further embodiment, the device includes at least one viewing aperture, whereby adherence of the magnetic particles on the interior portion of the vial can be viewed without removing the reagent cartridge from the device.

In yet another embodiment, the device includes an integral timing device which can be manually activated upon placement of a container in the device or the container can activate a switch. The timing device can be analog, digital or an LCD which turns from, for example, red to green after a preset time period.

In accordance with another embodiment of the invention there is provided a magnetic particle-suspending device for suspending settled magnetic particles. The magnetic particles are contained in a fluid-containing container. The container has an interior portion and an exterior portion. The container further has an interior bottom portion and an interior side wall portion. The device includes a clip. The clip has two side portions and a connecting portion, wherein the connecting portion joins the two side portions. Additionally, the two side portions of the clip are biased together, whereby insertion of the container

between the two side portions generates a compressive force on the container, thereby securing the container therein. The device also includes at least one magnet disposed adjacent to the clip.

In accordance with another aspect of the present invention there is provided an automated assay apparatus. The apparatus uses at least one fluid-containing container, that also contains magnetic particles. The container has an interior portion and an exterior portion. The container also has an interior bottom portion and an interior side wall portion. The apparatus comprises a container storage area. The container storage area including means for receiving the container. The improvement comprises at least one magnet positioned adjacent to the means for receiving the container, whereby the magnet causes at least some of the magnetic particles in the container to be adhered on an interior portion of the container, other than an interior bottom portion of the container.

In a particular embodiment, the apparatus uses a fluid-containing container, which is a reagent cartridge. The cartridge has a first side portion, a second side portion, a top portion, a base portion, a forward portion and a rear portion. The cartridge contains magnetic particles contained in a fluid-containing vial.

The vial has an interior portion and an exterior portion. The vial further has an interior bottom portion and an interior side wall portion.

In a particular embodiment, the means for receiving the reagent cartridge comprises at least two spaced apart plates defining therebetween a slot for the reagent cartridge.

In another embodiment, the at least one magnet is positioned on the plate and facing the slot. The apparatus further comprises a second magnet disposed opposite the at least one magnet, wherein the polarity of the second magnet disposed opposite the at least one magnet, and the polarity of the at least one magnet are the same with respect to the polarity directed to the magnetic particles.

In accordance with yet another aspect of the present invention there is provided a method for suspending magnetic particles that are contained in a fluid-

containing container. The container has an interior portion and an exterior portion. The container also has an interior bottom portion and an interior side wall portion. The method includes the steps of positioning at least one magnet adjacent to a portion of the container, other than the bottom portion, wherein the position of the magnet allows the magnetic force exerted by the magnet to attract the magnetic particles in the container to the magnet, whereby the particles are adhered to an interior portion of the container, other than an interior bottom portion. The method also includes the step of leaving the magnet adjacent to the portion of the container, other than the bottom portion, for a period of time sufficient to adhere at least some of the magnetic particles contained in the vial to the interior portion of the container; other than the bottom portion.

The method also includes the step of displacing the magnet from its position adjacent to the container before the particles become compactly adhered to the portion of the container other than the bottom portion, whereby the particles are easily suspended in the fluid.

In a particular embodiment the container is a vial. The vial is contained in a cartridge. The cartridge has a first side portion, a second side portion, a top portion, a base portion, a forward portion and a rear portion.

In another embodiment, the vial is rotatable within the cartridge. The method further includes the step of rotating the vial during the time which the magnet is positioned adjacent to a portion of the vial, other than the bottom portion.

In still another embodiment, the vial is rotatable within the cartridge. The method further includes the step of rotating the vial after the magnet has been displaced from its position adjacent to a portion of the vial, other than the bottom portion.

Other features and advantages of the invention will become apparent from the following detailed description, taken in conjunction with the accompanying

drawings, which illustrate, by way of example, various features of preferred embodiments of the invention.

Description of the Figures

The detailed description of the invention will be made with reference to the accompanying drawings, where like numerals designate corresponding parts of the figures. The drawings are meant to be generally illustrative of various examples of the present invention, but are merely examples and are not meant to be limiting of the scope of the invention.

FIG. 1 illustrates a broken-apart perspective view of one embodiment of a magnetic particle-suspending device of the present invention.

FIG. 2 illustrates a side view of one embodiment of a magnetic particle-suspending device of the present invention

FIG. 3 illustrates a top view of one embodiment of a magnetic particle-suspending device of the present invention

FIGS. 4A-4C illustrate a particular reagent cartridge which can be used with the presently claimed devices, apparatuses and methods.

FIG. 5 illustrates an embodiment of an automated assay instrument that can be used with the presently claimed devices, apparatuses and methods.

FIG. 6 illustrates in greater detail a reagent cartridge receiving area illustrated in FIG. 5.

Detailed Description of the Invention

The devices, apparatuses and methods of the present claims are designed to be used with magnetic particle-containing containers. Most typically, such magnetic particle-containing containers are used in performing biochemical assays, particularly immunoassays. However, the present claims are not limited to such applications, any magnetic-particle containing container, in which it is desired that magnetic particles be magnetically moved from one position in the container to another position in the container, in order to facilitate the unsettling and/or deagglutination of the particles and/or the ultimate suspension of the

particles in a fluid contained in the container are within the scope of the present claims.

The magnetic particle of the present invention can include a particle comprised of, but not limited to: a magnetic and/or magnetically influencable material alone or in combination with any one or more of the following, but not limited to: glass, latex, plastic, metal. Such a particle can have a size of from about 0.01 microns to about 20,000 microns, more preferably from about 0.05 microns to about 100 microns, and most preferably from about 0.05 microns to about 10 microns. In a preferred embodiment, the magnetic particle, is a superparamagnetic particle, as are known in the art. Superparamagnetic particles, while not themselves magnetic, have dipole moments and can be acted upon by a magnetic field.

Typically, about 5 ug to about 100 ug of magnetic particles are contained within a vial contained within a reagent cartridge that can be used with the present invention. However, containers containing larger amounts of magnetic particles are within the scope of the claims, as are containers of different sizes, because as the size of the device, and the size, number and strength of magnet used could be determined, with the teaching of this specification, by one of ordinary skill in the art, without undue experimentation.

The term particle is not meant to be limited to a particular shape of particle. For example, spherical, irregularly shaped, flat discs, solid bodies, perforated bodies and combinations of the above are within the scope of the present invention.

In a particular embodiment, the magnetic particle can be associated with a specific-binding moiety. The specific-binding moiety can be integral to the particle, such as a surface feature(s) that allows the particle to preferentially bind with other moieties or the particle can have associated with it the specific-binding moiety. Such specific-binding moieties include, but are not limited to: antibodies, lectins, and proteins, such as but not limited to streptavidin, avidin and avidin derivatives.

FIG. 1 illustrates a magnetic particle suspending device 600 for receiving a cartridge of the type, for example, illustrated in FIGS. 4A-C. The device 600 optionally includes a base 640, having cushioning pads 642a-d attached thereto. Base 640 can be affixed to a means for positioning the cartridge 620 by screws 644 and 645. Other affixation means can be used. Alternatively, base 640 can be integrally formed with cartridge positioning means 620.

Cartridge positioning means 620 includes a slot 621 adapted to receive a reagent cartridge. Cartridge positioning means 620 can be formed of, for example, metal, preferably non-magnetic such as aluminum, plastic, wood and combinations thereof. Preferably, the material is chemically inert, durable, easily machined, and inexpensive. One such material is acrylonitrile-butadiene-styrene. Slot 621 is formed by first side portion 622 and second side portion 623. First side portion 622 and second side portion 623 each include a surface 625 and 626, respectively, opposable against and shaped for at least partial mating engagement with a side portion of the cartridge. Cartridge positioning means 620 also includes a rear portion 624, which includes a surface 624 opposable against and shaped for at least partial mating engagement with a front or rear portion of the cartridge. First side portion 622 and second side portion 623 each include a slot 629 and 628, respectively, which each receive a magnet-retaining plate 630 and 632, respectively. Slot 628 and 629 each contain four holes adapted to receive one of magnets 610-617. Magnet-retaining plates 630 and 632 are held in place in slot 628 and 629 by screws 633-636 as illustrated. Optionally, an information-containing label 650 may be affixed to device 600. It is to be understood that different configurations of device 600 are within the scope of the claims. For example, magnet-retaining plates 630 and 632 may be dispensed with and the magnets held in position by adhesives or screws. And the number, type and configuration of a magnet or magnets used can differ, as described in more detail below.

In a particular embodiment, material, as known in the art, which shield magnetic fields can be applied around the magnets or a magnetic shield cover can be placed over the entire device.

In another embodiment, the device can contain at least a second slot formed by addition of a third side portion. Additional multiple-slot configurations are within the scope of the claims.

In yet another embodiment, the device can be used with a reagent cartridge that includes a vial which includes a means, such as a circular gear, for engaging a driving means, such as a rack gear. The device can include such a rack gear or a circular gear which can rotate the vial as the magnetic force is applied to, for example, the side wall of the vial. Such a driving gear can be placed adjacent any one of walls 622, 623 or 624 and held in place with, for example, a screw which allows for rotation of a circular gear or for lateral movement of a rack gear.

In still another embodiment, the device can be used with a reagent cartridge that includes a vial that is rotatable within the cartridge. The vial may optionally include a means, such as a circular gear. The device can include a slot allowing access to the gear. A person can access the vial including the gear, with a finger and apply a rotation to the vial as the magnetic force is applied to, for example, the side wall of the vial. Such a slot can be formed in any one or more of wall 622, 623 or 624.

In a further embodiment, the device can include at least one viewing aperture, whereby adherence of the magnetic particles on the interior portion of the vial can be viewed with the reagent cartridge in place in the device. Such a viewing aperture can be formed by a slot in for example wall.624, at a position which allows a view of the sidewalls of the vial at the level the magnets will cause adherence of the magnetic particles to the sidewall. The slot can be left open or include a transparent material such as glass or plastic.

In yet another embodiment, the device can comprise a clip having two side portions attached by a connecting portion and which through spring action can be

secured to a container containing magnetic particles. At least one magnet disposed adjacent to the clip for example affixed to at least one side portion of the clip provides for adherence of magnetic particles on an area of the container adjacent to the magnet.

With respect to the magnets, different shapes, such as but not limited to rectangular, toroidal, polygonal, circular, spherical and combinations thereof are within the scope of the claims.

A single magnet can be used, although at least two magnets separated by an arc of at least about 10 degrees is preferred and most preferably a pair of magnets is directly opposed, i.e. separated by an arc of about 180 degrees.

Alternatively, a single magnet shaped to encompass an arc of the vial of from about 10 degrees to about 360 can be used.

Alternatively, a number of magnets can be positioned around the device, for example four magnets separated by 90 degrees or 12 magnets separated by 30 degrees. Irregular spacing of the magnets is also within the scope of the invention.

When two, or more magnets are used, in a preferred embodiment, the polarity, typically designated north or south or plus (+) and minus (-), of directly opposing magnets, directed to the cartridge should be same. For example, as illustrated in Figure 2, magnet 614 has a positive polarity directed outward and therefore a negative polarity directed to the cartridge. Therefore, magnet 610 that opposes magnet 614, as seen in FIG. 1, should have a positive polarity directed outward and a negative polarity directed to the cartridge. The opposite configuration of these two magnets, i.e., positive polarity inward, negative polarity outward is also preferred. However, directly opposing magnets each with a different polarity directed to the cartridge are within the scope of the claims.

In another embodiment, a magnet can be positioned within the vial, for example it can be pivotably suspended from any one or more of walls, 622, 623 or 624. In this embodiment, the term "interior portion of the vial" includes the central portion of the vial and a magnet inserted therein.

The magnet used can be a permanent magnet as are known in the art or an elctromagnet as are known in the art.

The magnet or magnets can be formed of any material, such as but not limited to an iron magnet a ferrite-based ceramic, an alloy containing, for example, two or more of iron, cobalt, nickel and aluminum, such as an Aluminum-Nickel-Cobalt magnet, or rare earth containing alloy magnets, such as neodymium-iron-boron or samarium cobalt. The rare earth containing alloys are preferred, as they provide a strong magnetic field and are economical. Rare earth alloys containing neodymium are particularly preferred as they are less expensive than, for example, samarium-containing magents, and do not rust as easily as other rare earth alloy magnets.

The strength of the magnets used is from about 0.01 to about 1 Tesla. More preferably, from about 0.1 to about 0.8 Tesla and most preferably from about 0.3 to about 0.4 Tesla. At 0.3 Tesla the time to adhere the particles to the side walls of a container is about 30 second to a minute. As the Tesla decreases, this time will increase. At strengths over about 1 Tesla, there is a risk of too compactly adhering the particles to a portion of the container they were not previously settled against. However, this varies with the container the particles and therefore field strengths of over 1 Tesla can be used, if the readherence compaction problem does not occur.

The top view provided by FIG. 3 allows for a clear description of the positioning of the cartridge in device 600. When the cartridge is inserted in slot 621, and positioned against a surface opposable against and shaped for at least partial mating engagement with a front or rear portion of the cartridge 624, the vial contained in the cartridge is positioned in proximity to magnets 610-617, so that magnetic particles settled and/or agglutinated on the bottom of the vial are magnetically adhered to a side portion of the vial within the magnetic field of magnets 610-617. It is to be understood that the term "bottom of a vial" or "bottom of a container", is made with respect to the effects of gravity, or with respect to a previously applied magnetic field. Therefore, if a container had been

stored, for example, upside down, and particles had settled in a top portion of the container, for purposes of the invention, the top portion would be equivalent to a bottom portion of the container. Further, while it is preferred that the particles be adhered to a side portion of the container, their adherence to any other interior surface which has the effect of unsettling and/or deaglutinating the magentic particles is within the scope of the present invention. For example, in a particular aspect, a vial having a sealed top can be used with the device of the present invention. A magnet can be positioned to cause adherence of magnetic particles to this top portion of the vial.

Any configuration of surfaces which allow for the repeatable fixed positioning in three dimensions of a cartridge in relation to a magnet are within the scope of the claims. For example, surfaces which engage both: a) a side portion of the cartridge and a front portion of the cartridge; or b) a side portion of the cartridge and a rear portion of the cartridge; or c) a top portion of the cartridge and a front portion of the cartridge; or d) a top portion of the cartridge and a rear portion of the cartridge; or e) a bottom portion of the cartridge and a front portion of the cartridge; or f) a bottom portion of the cartridge and a rear portion of the cartridge; or g) a side portion of the cartridge and a top portion of the cartridge; or h) a side portion of the cartridge and a bottom portion of the cartridge; or i) a top portion of the cartridge and a bottom portion of the cartridge.

In a particular embodiment, a side portion of the cartridge and a bottom portion of the cartridge or a side portion of the cartridge and a top portion of the cartridge can be engaged by a surface opposable against and shaped for at least partial mating engagement therewith, wherein the device further includes a means of engaging either the side portion and/or the top portion and/or the bottom portion of the cartridge in a fixed position relative to the magnet. For example, instead of surface 624, to fix the position of the cartridge, a hinged arm can be affixed to wall 622 or 623. The arm when placed in an upward position will allow insertion of the cartridge into slot 621, although in this particular embodiment, wall 623 is not necessary, nor is slot 621 formed thereby. The

position of the cartridge is then adjusted until the arm can be lowered to engage, for example, an orifice in the cartridge, such as 494 as depicted in FIG. 4A. The cartridge is thereby held in fixed position relative to the magnet.

Most preferably, the surfaces allow for repeatable fixed positioning of the cartridge in relation to the magnet, so that the magnet can exert a maximum magnetic field on, for example, the side portion of the magnetic particle-containing vial. However, different devices can be configured so that the fixed position of the cartridge with respect to the magnet can be adjusted to provide less than maximum magnetic field strength at the vial walls.

In a particular embodiment, the fixed position of the cartridge in relation to magnet can be adjustable within the same device so that that the fixed position of the cartridge with respect to the magnet can be adjusted to provide less than maximum magnetic field strength at the vial walls. In this embodiment, the term fixed means the cartridge is held stationary in a repeatable position for some period of time, and then can be held stationary in at least one other repeatable position for some period of time.

FIG. 4A depicts a reagent cartridge 432 suitable for use with the presently claimed device, apparatus and methods. Other reagent cartridges for use in the presently claimed device, apparatus and methods are within the scope of the present claims. The cartridge 432 in general is an elongate prismatic body 434 consisting of a base portion 436, and one or more removably attached add-on portions 438, each molded of polymer material. The cartridge has a first side portion 400, a second side portion 402, a top portion 404, a base portion 436, a forward portion 440 and a rear portion 410. At the forward portion 440 of the base portion 436, the base portion 436 defines a vertically extending bore 442 in which an agitation container 444 is rotationally received captively. The agitation container 444 includes an upper radially extending flange portion 446, which is disposed adjacent to an upper flange portion 448 of the body 434. A molded resilient integral hook portion 450 extends from the flange 448 over flange 446 to captively retain agitation container 444 in the bore 442. In an alternative

embodiment, the vial can be retained by a flexible flange which extends beneath gear 456 and through the collar depicted in space 454. The body 434 has a lower edge 452, which at the forward portion 440 of the module bounds an opening 454. Agitation container 444 includes circumferentially continuous gear portion 456 exposed in this opening. Above the opening 454, the body 434 includes sensor tab 458, which is receivable into a sensor opening 460 at the rear of recess 416 to inform a computer system on an automated assay instrument (not shown) where a particular reagent module has been inserted into the slots 430. Above the sensor tab 458, the body 434 includes a pair of spaced apart resilient detent tongues 462. These tongues are receivable on opposite sides of a positioning key 464 at the rear of a recess, Se FIG. 6, and engage opposite detents, see FIG. 6, to removably retain cartridge 432 in a particular slot, see FIG 6.

Internally, agitation container 444 includes vertically extending agitation fins 472, see FIG. 4C, so that rotary oscillation of this container effected by reciprocation of a rack (not shown) stirs the contents of container 444. Container 444 is used to hold a reagent liquid which includes solid-phase particles, such as magnetic particles. The agitation of this container prevents the beads from settling, so that they may be transferred along with the liquid contained therein into a container, such as a cuvette, by a probe of an automated assay instrument (not shown). Container 444 includes a slit septum, 474, as shown in FIG. 4C. Base portion 436 further includes three recesses 476, within which respective reagent containers 478 are removably received. The reagent containers 478 each include a slit septum 478' closing the top opening of these containers, but through which a probe (not shown) may access the reagent liquid in these containers. At the rear of base portion 436 is defined a pair of vertically extending spaced apart guide rails 482. The guide rails 482 cooperate with the remainder of body 434 to define a pair of oppositely opening vertically extending grooves 484, each ending vertically upwardly at an abutment surface 486 adjacent to the upper flange 448 of body 434. The add-on portion 438 has a pair

of elongate vertically extending inwardly facing engagement tongues 448, which are vertically receivable in sliding engagement into the grooves 484. Add-on portion 438 includes a lid 490 defining an opening 492 closed by slit septum 494 by which the probe (not shown) may access the liquid reagent in these add-on portions 438.

Add-on portions 438 at their side opposite the base portion 436 define features replicating those of the base portion, so that additional add-on portions may be interlocked to form the regent cartridges 432, as is indicated in phantom lines, viewing FIG. 4A. Either the base portion 436 or add-on portions 438 may accept a handle member 496 and be configured with engagement tongues like those referenced above with respect to numeral 488. This handle member 496 is engageable with the base portion 436 or with one of the add-on portions 438 in order to facilitate manual grasping and easy insertion and removal of the reagent cartridges 432 at slots 430. At a side surface 498, reagent cartridge 432 can carry a bar code tag 500, which allows for identification by the assay instrument, see FIG. 5, of the particular reagents provided to the instrument in each cartridge 432.

FIG. 5 depicts an example of an automated assay apparatus 10 that is within the scope of the claims. The apparatus 10 includes housing 12. The housing 12 includes a base portion 14, including a shelf-like upper surface 16 defined in part by removable upper covers 18, and an upstanding rear portion 20. The upper surface 16 also encompasses several open areas. Upwardly, the area within guardrail 22 is open, and a pair of arms 26 and 28 extends forwardly from the rear portion 20 over the upper surface 16. Arms 26 and 28 are laterally movable in then x direction as indicated by arrows 26′ and 28′ along the rear portion 20 and over surface 16. Each arm 26 and 28 carries a respective probe portion 30, vertically movable in the z direction, as indicated by arrow 29′. This probe portion is also movable front to rear along the arms 26 and 28 in the y direction as indicated by arrow 30′. Accordingly, it is seen that the probes 26 and 28 can access virtually the entire upper surface 16 of the base portion 14.

The apparatus is interfaced with a computer system 32 by a cable 34. Computer 32 may be any one of several commonly available personal computers and may interface with other personal or mainframe computers. Typically, the apparatus 10 includes on-board processing capability interfacing with computer system 32 in order to control and monitor the operation of apparatus 10, as well as collect and report the results of assays such as immunoassays, particularly chemiluminescent assays carried out.

In general the apparatus 10 receives liquid samples, such as patient samples for medical diagnostic testing, in tubes at a sample area 42 and at a receiving area 44 receives disposable cuvettes 45, which each include plural recesses (not shown) for receiving respective aliquots of sample liquid transferred by the probe 30 on arm 26. The present invention is not limited to an apparatus that uses a particular design or configuration of cuvette.

At a reagent area 46, shown in detail in FIG. 6, the apparatus 10 receives reagents in modular receptacles, such as reagent cartridges, as illustrated in FIGS. 4A-4C, which contain at least one container including magnetic particles, and transfers aliquots of reagents by the probe arm 30 on arm 28 to certain of the recesses in cuvette 45 in order to conduct assays. These magnetic particles which can have become settled on the bottom of the reagent cartridge vial, must be suspended in the fluid contained in the vial before the probe arm accesses the vial in order to transfer an aliquot of magnetic particle-containing fluid to the cuvette.

FIG. 6 depicts reagent area 46 in more detail. The reagent area 46 includes a plate portion 426 having a plurality of spaced-apart plates 428 defining threbetween a plurality of slots 430 for individually receiving a reagent cartridge 432. In one particular embodiment, reagent area 46 includes a recess 416 spanned by perforate cover portion 18 with plural apertures 418 through which probe 30 of arm 28 can access reagent materials stored in area 46. Cartridge 432 includes detent tongues 462 that are receivable on opposite sides of positioning key 464 and engage opposed detentes 466 to removably retain

cartridge 432 in a slot 430. A sensor tab 458, see FIG. 4A, is receivable into a sensor slot 460. Below sensor slots 460 there is provided a reciprocable rack member 468 engageable with the gear portion 456 of cartridge 432 inserted into slot 430. The rack member 468 is reciprocated by a drive motor 470.

The presently claimed apparatus includes at least one magnet disposed adjacent to the reagent cartridge storage area. The at least one magnet is disposed adjacent the reagent cartridge so that the magnetic field it produces will adhere magnetic particles contained in, for example, a vial in the reagent cartridge, to an interior portion of the vial other than the bottom portion of the vial. For example, the magnet 490 can be affixed to rear wall 491 of slot 430 or magnet 492 can be affixed to plate 426, so that it is adjacent to the sidewall of the vial containing the magnetic particles. Other configurations of magnets that accomplish this magnetic suspension are within the scope of the claims. For example, an entire plate, or some portion of the plate can be comprised of a magnet.

In one embodiment, a magnet is present on every plate so that a cartridge in every slot is adjacent to two magnets. In an alternative embodiment, less than all the plates contain magnets. Accordingly, a cartridge can be placed in a slot containing at least one magnet, for a period of time, and then be removed from the slot and hence the influence of the magnet, thereby allowing the particles adhered to the walls of the vial to begin to go into suspension. Alternatively magnets which may be easily repeatedly placed by the cartridge and then removed can be used. In yet another embodiment, an electromagnet that is selectively magnetizable can be used. Upon magnetizing the magnetic particles will be adhered to the side walls. Upon cessation of the magnetization of the electromagnet, the particles can begin to suspend in the fluid contained in the container. In a further embodiment, the electromagnet can be switched on and off, or opposed electromagnets can be alternatively turned on and off, to provide a vigorous, changing magnetic force to the magnetic particles. The magnet containing slot can be accessible to the rack member 468 or isolated therefrom.

The cartridge can then be inserted into a slot which is accessible to rack member 468. The rotation to the vial provided by the rack member can assist in the suspension of the particles from the side wall of the vial into the fluid contained therein.

In another embodiment a space can be left in reagent area 46 for placement of the device described in FIGS. 1 and 3. This provides a convenient method of suspending the particles and then having quick access to the cartridge to remove the cartridge from the device and insert the cartridge into a slot 430.

Apparatus for automated assays that use the magnetic suspension devices as described herein, can be originally fabricated or existing apparatus that do not contain the magnetic suspension devices as described herein can be so modified.

An example of an automated apparatus on which assays, using magnetic particles which may require suspension from a settled state and which can be modified as described herein, is the Nichols Advantage,™ automated assay platform, available from Nichols Institute Diagnostics, San Juan Capistrano, California. It is to be understood that other automated instruments, using containers having magnetic particles that must be transferred from a settled to a suspended state are within the scope of the claims.

EXAMPLE 1 SUSPENSION OF MAGNETIC PARTICLES

A particular batch of Bangs® magnetic particles contained in a fluid-containing vial that had remained undisturbed for over one year, was placed in the device of the present invention. Due to the effects of gravity the magnetic particles had compactly settled to the bottom of the vial. Within one minute of placement in the device, particles were adhered to the side wall of the vial. The vial was then placed on an automated assay instrument which provided gentle rotational agitation to the vial. After five minutes on the apparatus, almost all the particles were suspended in the fluid. Without use of the device, but resort to the rotational agitation provided by the automated assay instrument, the particles were not suspended in the fluid even after about one hour.

EXAMPLE 2 PARTICLE MULTISIZER DETERMINATION OF PARTICLE HOMOGENEITY

Both Seradyne® and Bangs® magnetic particles were used in this resuspension study.

One sample of magnetic particles contained in a fluid-containing vial was vortexed to ensure thorough suspension of the particles in the fluid. A reading of the concentration of the particles in suspension was deteremined on a Coulter multisizer, at time= 0, time=20 minutes and time= 60 minutes to obtain a baseline of full suspension for comparison. Another sample, sample of magnetic particles contained in a fluid-containing vial was placed in the device presently claimed and reading taken at time = 1minute, and time = 5 minutes. It was observed that in 2-5 minutes readings indicating full suspension of the magnetic particles were obtained.

EXAMPLE 3 COMPARISON OF MAGNET POLARITY CONFIGURATIONS

12 different vials, half of Seradyne® and half of Bangs® magnetic particles, which had been undisturbed for over one year were tested in two devices as presently claimed. In device one, two pairs of opposed magnets were arranged one on top of the other. The positive pole of all four magnets was directed towards a vial placed in the device. The time, in seconds, until substantially all the magnetic particles contained in each of six vials placed therein were adhered to the sides is as follows: 26, 14, 18, 22, 15, 21, for an average of 19.3. In device two, two pairs of opposed magnets were arranged one on top of the other. The positive pole of the bottom two magnets was directed towards a vial placed in the device. However, with respect to the top pair, one magnets positive pole was directed in towards the vial and the other magnets negative pole was directed in towards the vial. The time, in seconds, until substantially all the magnetic particles contained in each of six vials placed therein were adhered to the sides is as follows: 32, 45, 63, 41, 73, 50, for an average of 50.7. Therefore, while both configurations of magnets provide a substantial improvement over mechanical methods of suspension, it appears that the best

method of magnetic adherence, allowing for subsequent suspension, occurs when the magnetic poles of opposite magnets directed towards the vial are the same.

The methods of the present invention may be performed as follows: A container having magnetic particles contained therein is provided by a person. A magnet, which need not be in the device but can be, or any magnet is positioned adjacent to the container to cause the magnetic particles contained therein to adhere to the sides of the container. The magnet is left in this position for a period of time sufficient to adhere at least some of the magnetic particles contained in the vial to the interior portion of the vial; other than the bottom portion. Importantly, the magnet is displaced from its position adjacent to the container before the particles become compactly adhered to the portion of the vial other than the bottom portion. Otherwise the particles can be almost as difficult to displace from the side wall as from the bottom, thereby interfering with the ultimate goal which is the suspension of the particles in the fluid. Preferably, the magnet is removed within about 10 minutes, more preferably within about 5 minutes, and most preferably within about one minute.

In one aspect of the present invention, the container can be a vial contained in a cartridge, wherein the vial is rotatable within the cartridge. The method further includes the step of rotating the vial during the time which the magnet is positioned adjacent to a portion of the vial, other than the bottom portion.

In another aspect of the present invention, the container can be a vial contained in a cartridge, wherein the vial is rotatable within the cartridge. The method further includes the step of rotating the vial after the magnet has been displaced from its position adjacent to a portion of the vial, other than the bottom portion.

In one embodiment, the vial contains interior vanes and these interior vanes are positioned by a person carrying out the method, so that magnetic particles adhere to the sidewall of the vial between the vanes and not on the vanes.

The presently disclosed embodiments are to be considered in all respects as illustrative and not restrictive, the scope of the invention being indicated by the

appended claims, rather than the foregoing description, and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced therein.

What is claimed is:

1. A magnetic particle suspending device for suspending settled magnetic particles, the magnetic particles contained in a fluid-containing vial, the vial having an interior portion and an exterior portion, the vial further having an interior bottom portion and an interior side wall portion, wherein the vial is contained in a cartridge, the cartridge having a first side portion, a second side portion, a top portion, a base portion, a forward portion and a rear portion, the device comprising:

a) at least one magnet disposed adjacent to the device, further wherein the magnet is disposed to provide a magnetic force on at least two separate points on the interior portion of the vial, and

b) means for positioning the cartridge and the magnetic particle containing vial in relation to the at least one magnet, wherein the positioning means provides for the repeatable, fixed positioning in three dimensions of a cartridge in relation to the magnet, whereby such positioned placement of the cartridge in the device causes at least some of the settled magnetic particles settled in the interior bottom portion of the vial to be adhered on an interior portion of the vial other than the interior bottom portion of the vial.

2. The device of claim 1 wherein, the two separate points are separated by an angle of from about 10 degrees to about 180 degrees.

3. The device of claim 1 wherein the means for positioning include at least one surface opposable against and shaped for at least partial mating engagement is selected from the group consisting of: a) a side portion of the cartridge and a front portion of the cartridge; or b) a side portion of the cartridge and a rear portion of the cartridge; or c) a top portion of the cartridge and a front portion of the cartridge; or d) a top portion of the cartridge and a rear portion of the cartridge; or e) a bottom portion of the cartridge and a front portion of the

cartridge; or f) a bottom portion of the cartridge and a rear portion of the cartridge; or g) a side portion of the cartridge and a top portion of the cartridge; or h) a side portion of the cartridge and a bottom portion of the cartridge; or I) a top portion of the cartridge and a bottom portion of the cartridge.

4. The device of claim 1 wherein such positioned placement of the cartridge in the device causes at least about 80% of the settled magnetic particles settled in the interior bottom portion of the vial to be adhered on an interior portion of the vial other than the interior bottom portion of the vial.

5. The device of claim 1 further comprising a second magnet disposed adjacent to the device.

6. The device of claim 5 wherein the second magnet is disposed opposite the at least one magnet.

7. The device of claim 6 wherein the polarity of the second magnet disposed opposite the at least one magnet, and the polarity of the at least one magnet are the same with respect to the polarity directed to the magnetic particles.

8. The device of claim 1 wherein the magnet is selected from the group consisting of a permanent magnet and an electromagnet.

9. The device of claim 1 wherein the device includes a feature selected from the group consisting of: magnetic shielding material, at least a second means for positioning the cartridge and the magnetic particle containing vial in relation to the at least one magnet, and wherein the fixed position of the cartridge in relation to the magnet is adjustable.

10. The device of claim 1 wherein the magnet is comprised of a material selected from the group consisting of iron, and alloys of at least two of the following: iron, cobalt, nickel and aluminum.

11. The device of claim 1 wherein the magnet is comprised of a ferrite-based ceramic magnet.

12. The device of claim 1 wherein the magnet is selected from the group consisting of an alloy of a) Neodmium and Iron and Boron or b) Samarium and Cobalt.

13. The device of claim 1 wherein the vial further includes a portion adapted to engage a drive means, the device further including the drive means for engaging the vial portion.

14. The device of claim 1 wherein the vial further includes a portion adapted to engage a drive means, the device further including a slot allowing access to the drive means.

15. The device of claim 1 further including at least one viewing aperture, whereby adherence of the magnetic particles on the interior portion of the vial can be viewed with the reagent cartridge in place in the device.

16. A magnetic particle suspending device for suspending settled magnetic particles, the magnetic particles contained in a fluid-containing container, the container having an interior portion and an exterior portion, the container further having an interior bottom portion and an interior side wall portion, the device comprising:

a) a clip, the clip having two side portions and a connecting portion, wherein the connecting portion joins the two side portions, further wherein the

two side portions of the clip are biased together, whereby insertion of the container between the two side portions generates a compressive force on the container, thereby securing the container therein; and

b) at least one magnet disposed adjacent to the clip.

17. The device of claim 16 wherein the magnet is selected from the group consisting of a permanent magnet or an electromagnet.

18. The device of claim 16 further comprising a second magnet disposed adjacent to the clip.

19. The device of claim 18 wherein the second magnet is disposed opposite the at least one magnet.

20. The device of claim 18 wherein the polarity of the second magnet disposed opposite the at least one magnet, and the polarity of the at least one magnet are the same with respect to the polarity directed to the magnetic particles.

21. In an automated assay apparatus, the apparatus using a fluid-containing container, the container containing magnetic particles, the container having an interior portion and an exterior portion, the container further having an interior bottom portion and an interior side wall portion, the apparatus comprising a magnetic particle container storage area, the container storage area including means for receiving the container, the improvement comprising at least one magnet positioned adjacent to the means for receiving the container, whereby the magnet causes at least some of the magnetic particles in the container to be adhered on an interior portion of the container, other than an interior bottom portion of the container.

22. The apparatus of claim 21 wherein the fluid containing container comprises a reagent cartridge, the cartridge having a first side portion, a second side portion, a top portion, a base portion, a forward portion and a rear portion, wherein the cartridge contains magnetic particles contained in a fluid-containing vial, the vial having an interior portion and an exterior portion, the vial further having an interior bottom portion and an interior side wall portion.

23. The apparatus of claim 22 wherein the means for receiving the reagent cartridge comprises at least two spaced apart plates defining therebetween a slot for the reagent cartridge.

24. The apparatus of claim 23 wherein the at least one magnet is positioned on the plate and facing the slot, the apparatus further comprising a second magnet disposed opposite the at least one magnet, wherein the polarity of the second magnet disposed opposite the at least one magnet, and the polarity of the at least one magnet are the same with respect to the polarity directed to the magnetic particles.

25. A method for suspending magnetic particles, the magnetic particles being contained in a fluid-containing container, the container having an interior portion and an exterior portion, the container further having an interior bottom portion and an interior side wall portion, the method comprising the steps of:

a) positioning at least one magnet adjacent to a portion of the container, other than the bottom portion, wherein the position of the magnet allows the magnetic force exerted by the magnet to attract the magnetic particles in the container to the magnet, whereby the particles are adhered to an interior portion of the container, other than an interior bottom portion;

b) leaving the magnet adjacent to the portion of the container, other than the bottom portion, for a period of time sufficient to adhere at least some of

the magnetic particles contained in the container to the interior portion of the container; other than the bottom portion and,

c) displacing the magnet from its position adjacent to the container before the particles become compactly adhered to the portion of the container other than the bottom portion, whereby the particles are easily suspended in the fluid.

26. The method of claim 25, wherein the container is a vial, further wherein the vial is contained in a cartridge, the cartridge having a first side portion, a second side portion, a top portion, a base portion, a forward portion and a rear portion.

27. The method of claim 26 wherein the vial is rotatable within the cartridge, the method further comprising the step of rotating the vial during the time which the magnet is positioned adjacent to a portion of the vial, other than the bottom portion.

28. The method of claim 26 wherein the vial is rotatable within the cartridge, the method further comprising the step of rotating the vial after the magnet has been displaced from its position adjacent to a portion of the vial, other than the bottom portion.

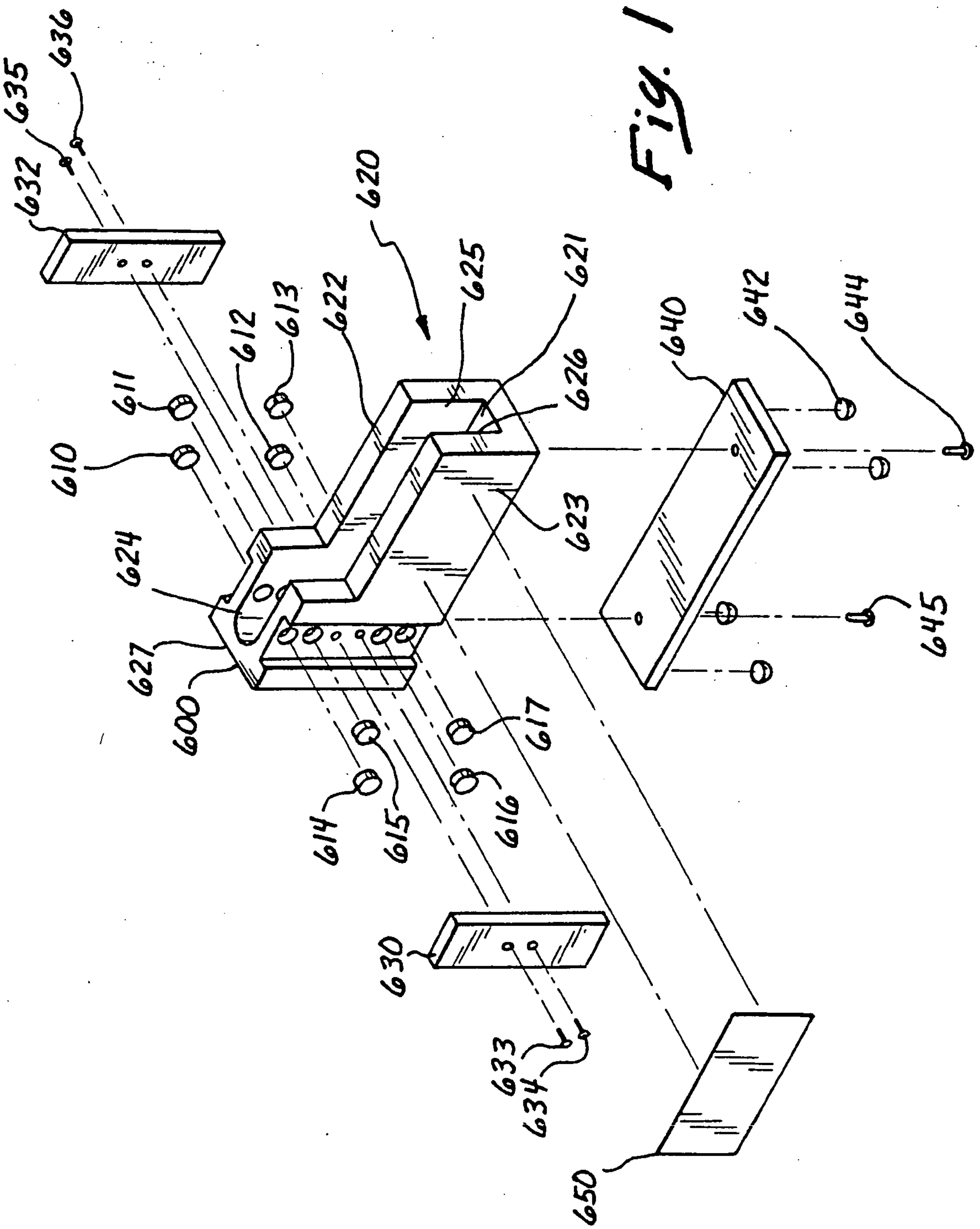
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Fig. 1

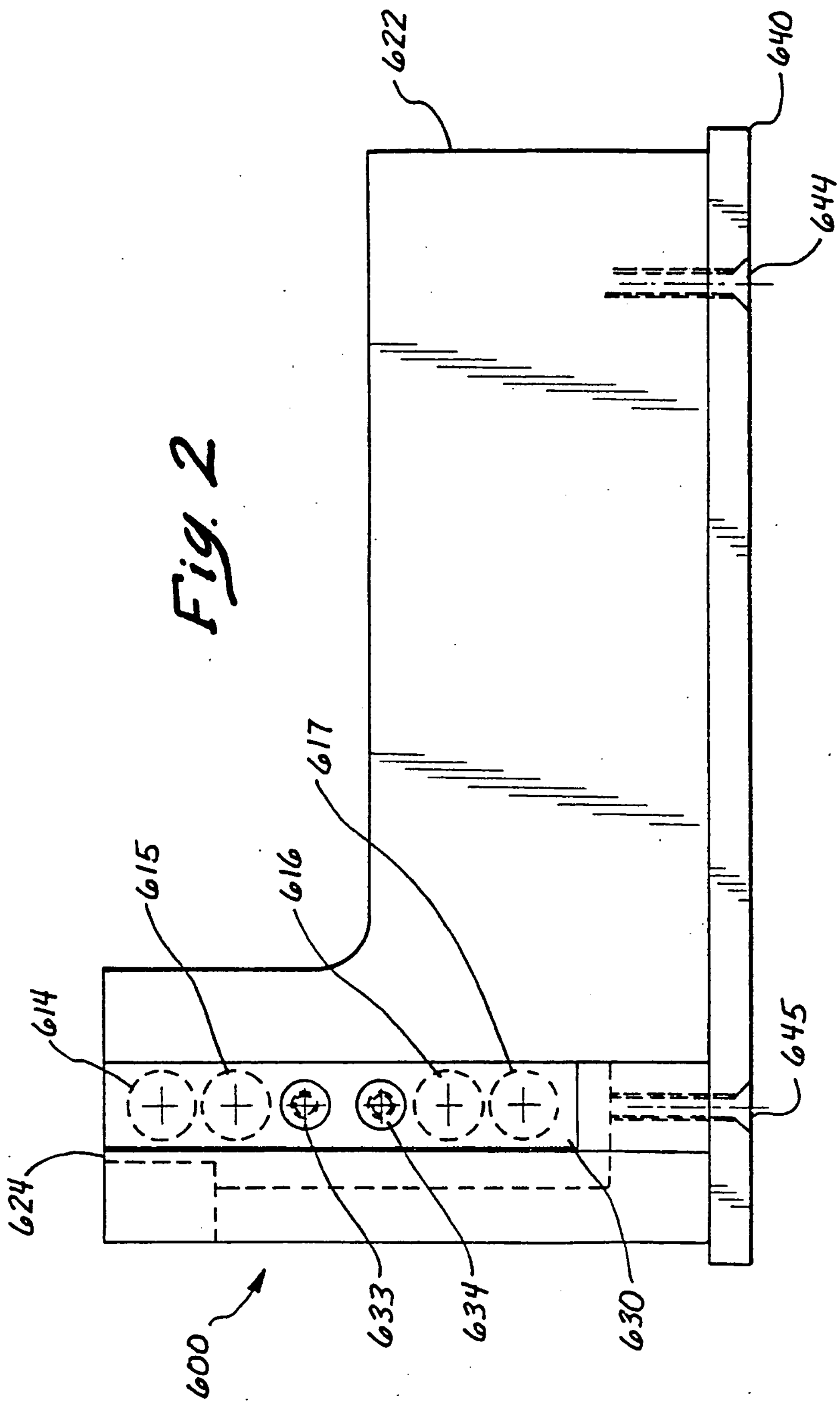

Fig. 2

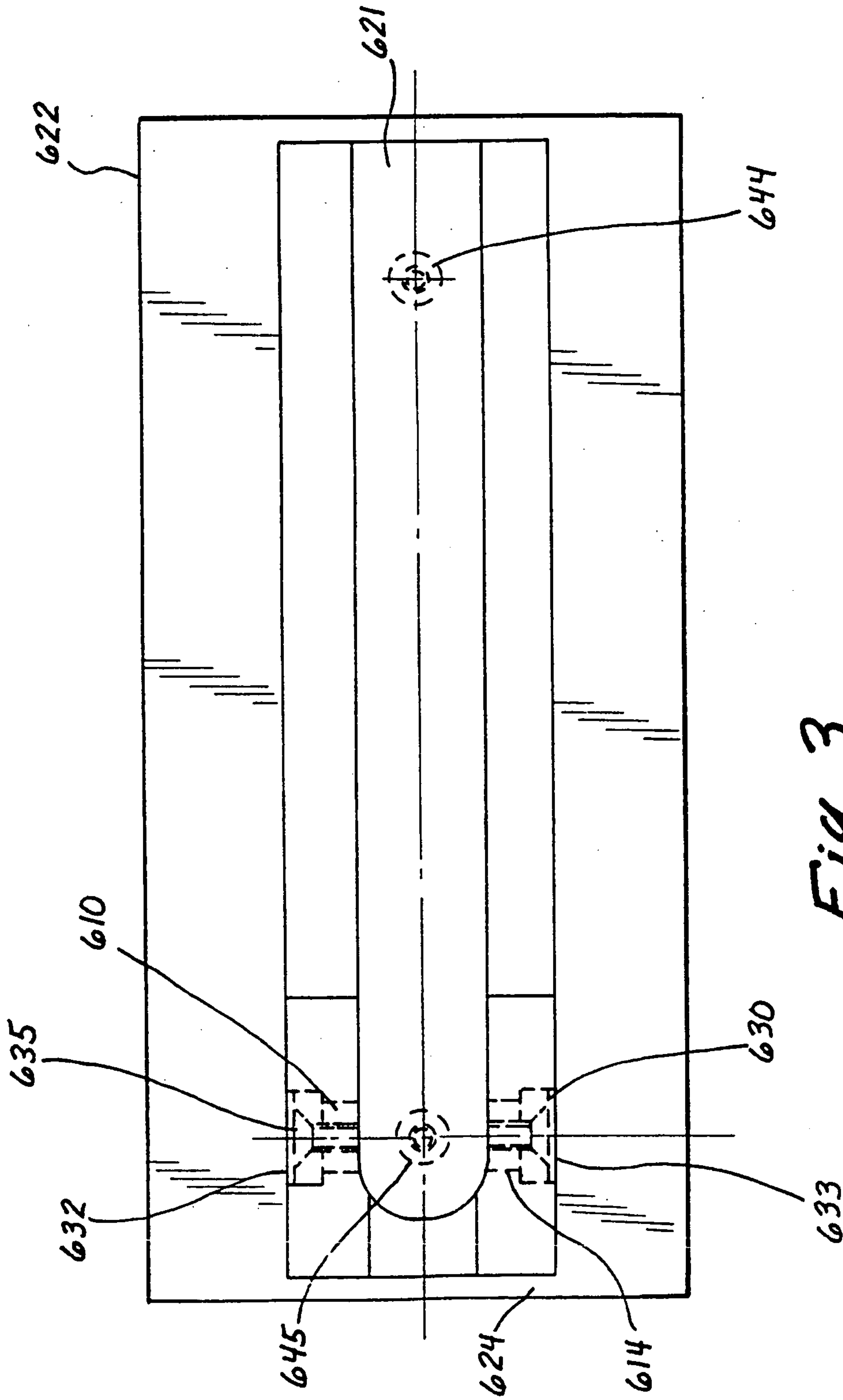

Fig. 3

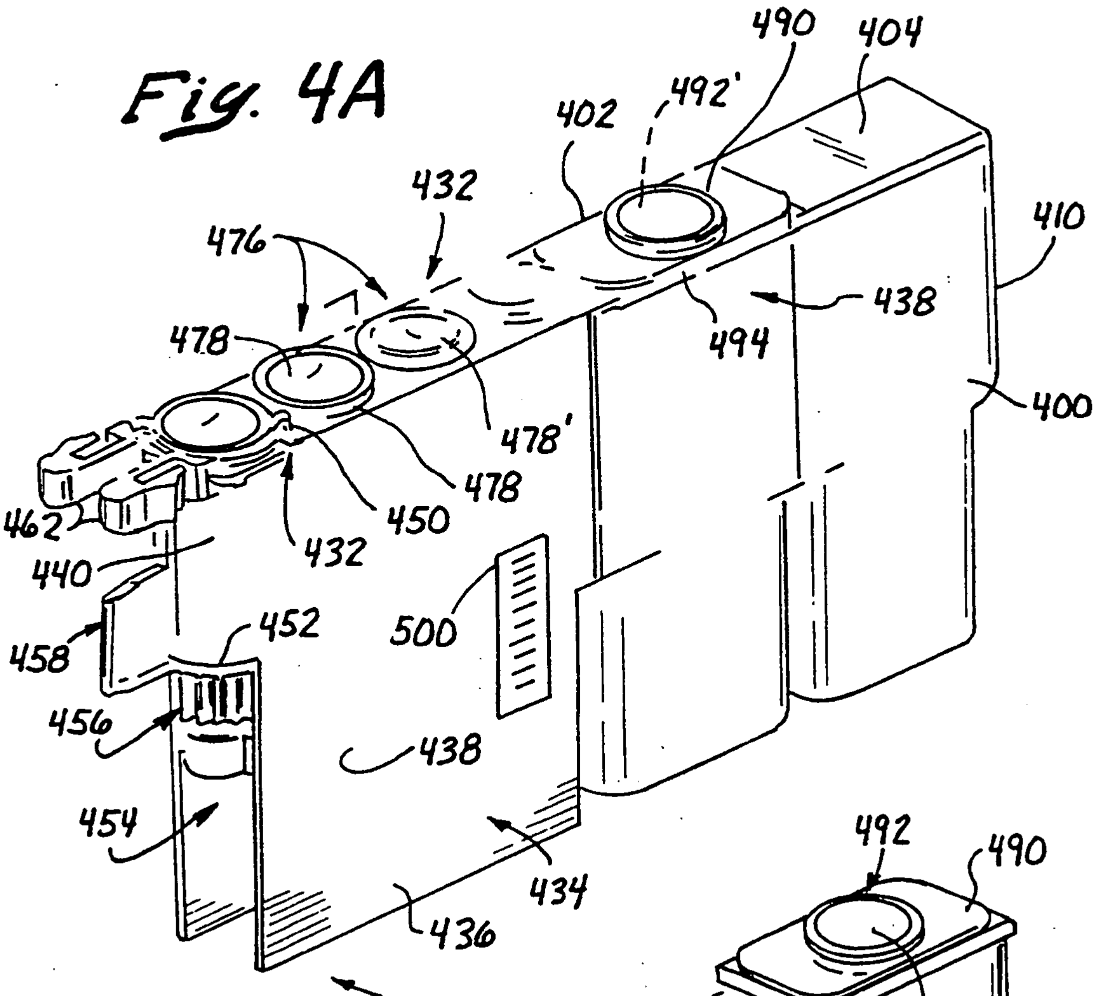

Fig. 4A

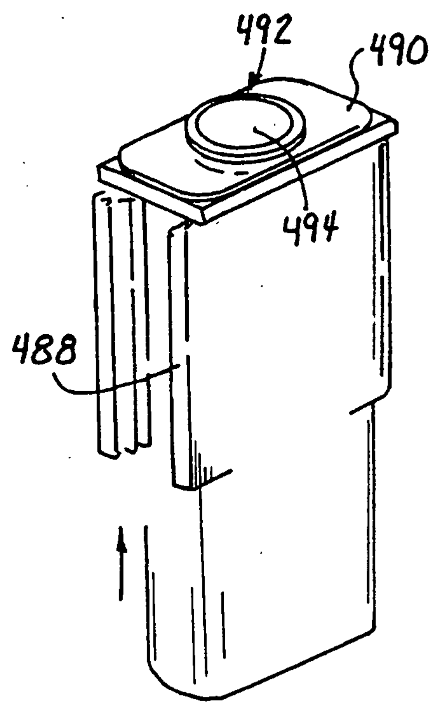

Fig. 4B

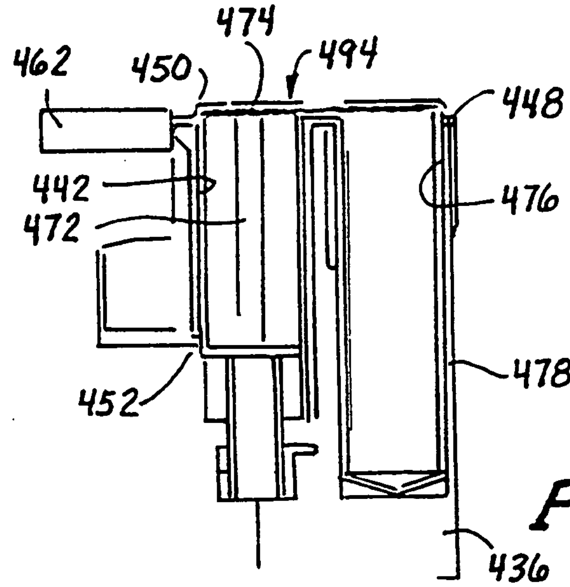

Fig. 4C

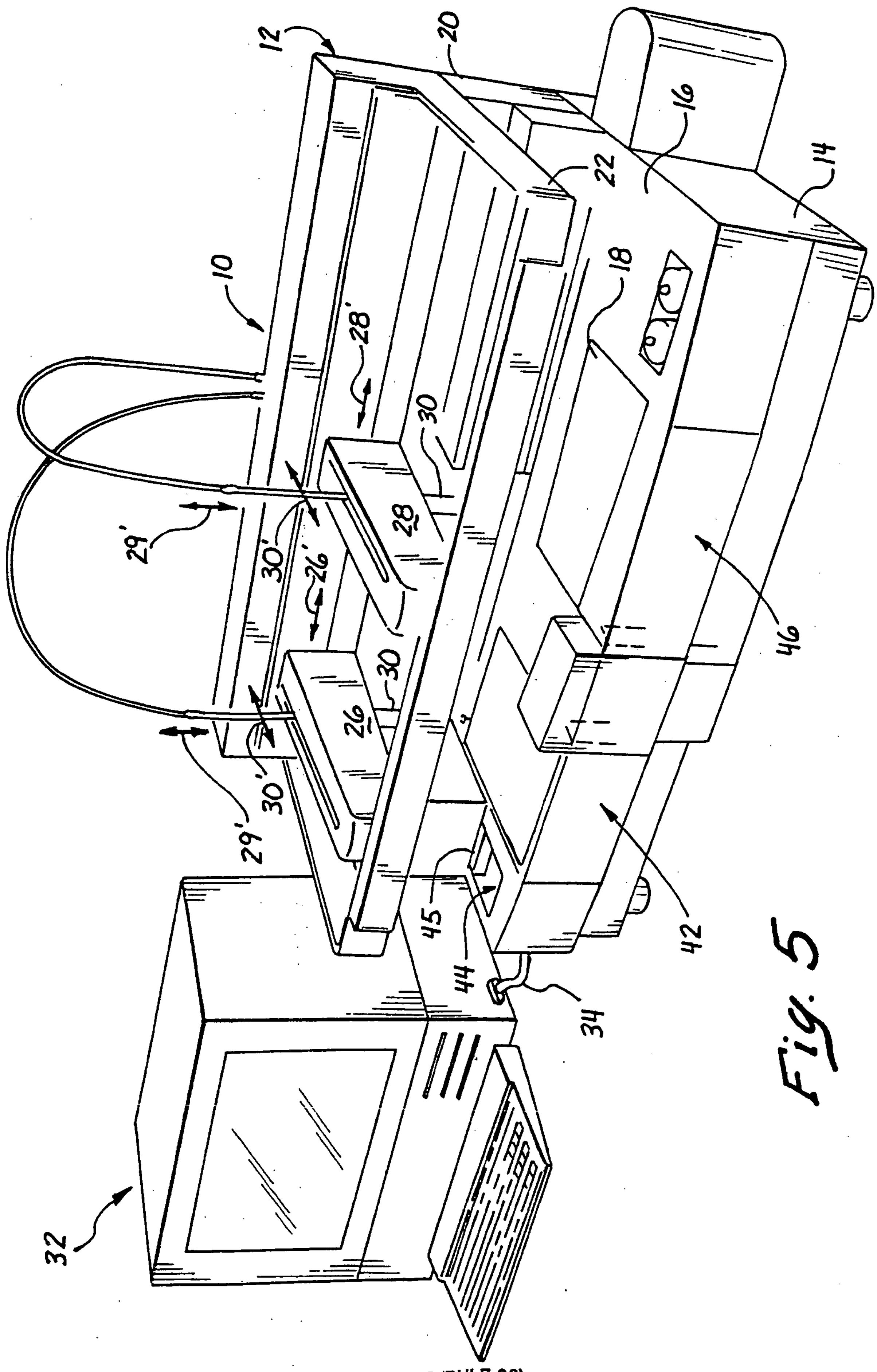

Fig. 5

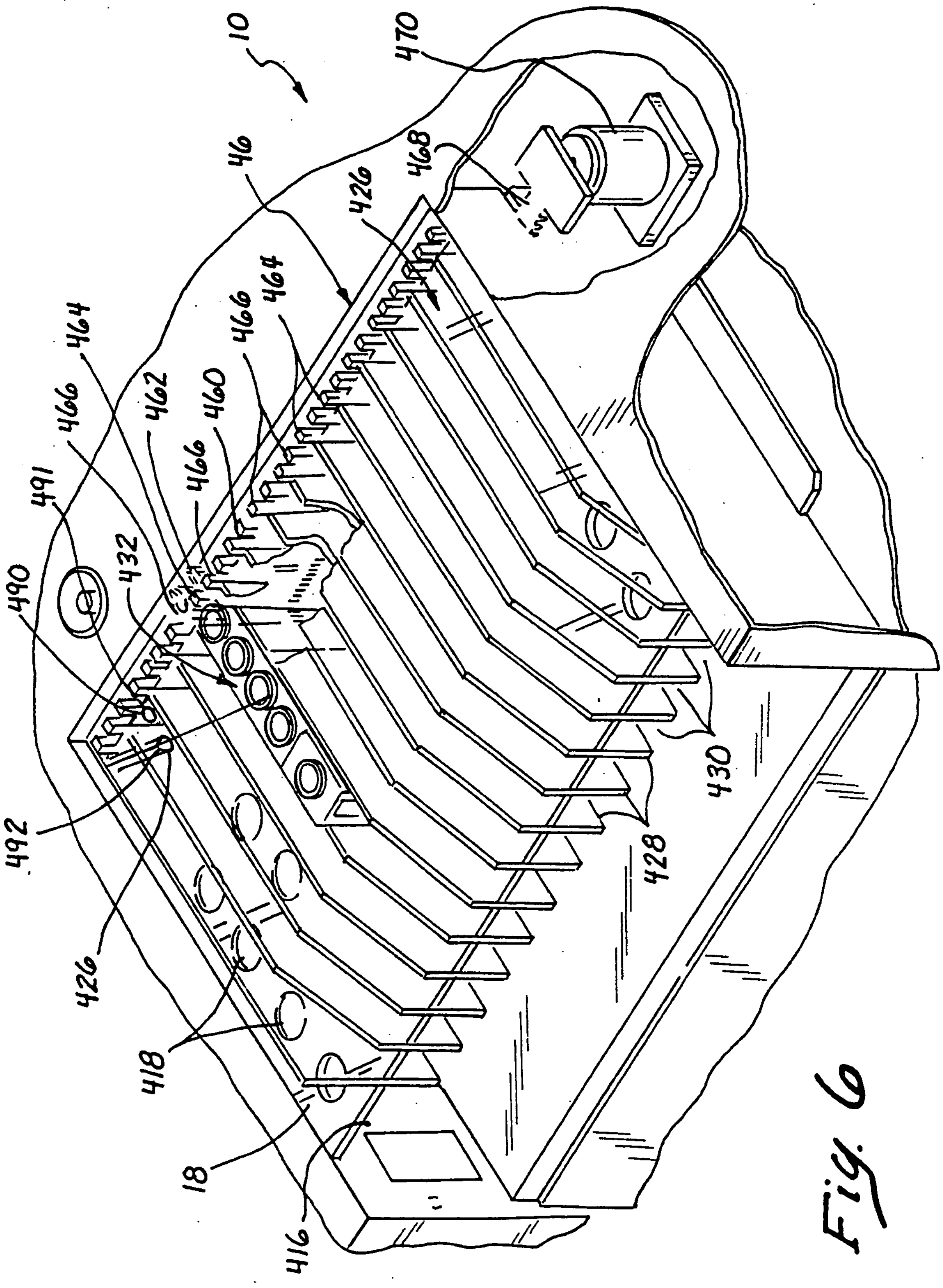
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Fig. 6